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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,460	09/28/2006	Yoko Yamagata	56861	9304

1609 7590 03/30/2012  
ROYLANCE, ABRAMS, BERDO & GOODMAN, L.L.P.  
1300 19TH STREET, N.W.  
SUITE 600  
WASHINGTON,, DC 20036

EXAMINER
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BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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03/30/2012

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/599,460	<b>Applicant(s)</b> YAMAGATA ET AL.
	<b>Examiner</b> Michael Burkhart	<b>Art Unit</b> 1633

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 08 March 2012 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

**NO NOTICE OF APPEAL FILED**

1. ☒ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires \_\_\_\_\_ months from the mailing date of the prior Advisory Action or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.

*Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANT'S FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).*

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because

a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);

b) ☐ They raise the issue of new matter (see NOTE below);

c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): (a) ☐ will not be entered, or (b) ☒ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☒ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
     See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement(s)*. (PTO/SB/08) Paper No(s). \_\_\_\_\_

13. ☐ Other: \_\_\_\_\_.

**STATUS OF CLAIMS**

14. The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1,7 and 8.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

	/Michael Burkhart/ Primary Examiner, Art Unit 1633
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Continuation of 11. does NOT place the application in condition for allowance because: Claims 1, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elgersma et al (Neuron, 2002), Wang et al (PNAS, 2003), Hanson et al (Neuron, 1994) and Sutoo et al (Brain Res., 2002). This rejection is maintained for reasons made of record in the Office Actions dated 7/9/2009, 2/18/2010, 6/7/2010, 3/29/2011, 11/9/2011, and for reasons set forth below.

#### Response to Arguments

Applicant's arguments filed 3/8/2012 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the claims recite unexpected results regarding the generation of CaMKIIalpha knock-in mice; 2) the combined disclosure of the cited art would not yield predictable results regarding generation of CaMKIIalpha knock-in mice.

Regarding 1) and 2), these assertions and opinions have been addressed at length in previous Office Actions. Applicants present nothing more in the line of actual evidence that generation of the claimed mice would be unpredictable. Such assertions are countered by the preponderance of facts and evidence provided by the prior art of record, published in peer-reviewed journals. Confusingly, applicants argue that generation of CaMKIIalpha knock-in or knock-out mice is an unpredictable technology, then supply further references wherein such mice are generated (e.g. Silva et al). There is no obvious barrier to targeting the exon of choice in the CaMKIIalpha gene (or literally any other well-characterized gene) given the totality of the prior art. Applicants are directed, again, to the results of Elgersma et al wherein mutant CaMKIIalpha knock-in mice are prepared and not associated with any difficulty in creation of the mice, or in breeding. Applicants are inventing problems that do not exist or have been solved by the prior art. That the generation of knock-out mice is easier to accomplish is not at all certain and not stipulated. Generally, knock-outs (removal of a protein or its activity) are a more drastic mutation having more profound effects on the viability and breeding of mice than the more subtle knock-in (e.g. changing one or a few residues)..